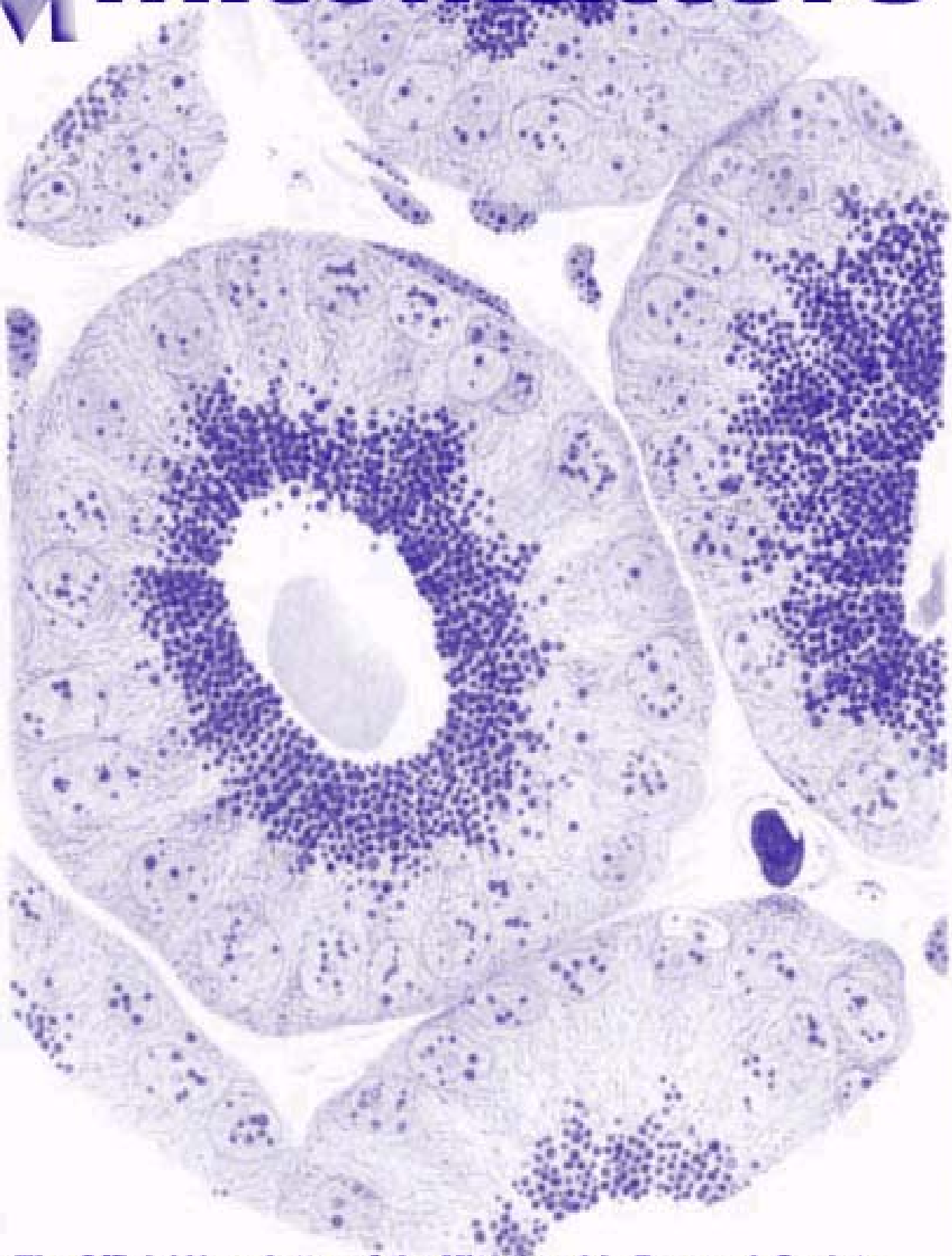
MitoMatters



The Official Newsletter of the Mitochondria Research Society

Vol 1, Winter 2002

Editor's Note

Welcome to the first issue of MitoMatters, the official newsletter of the Mitochondria Research Society (MRS). With this newsletter you will find the MRS 2002 application/renewal form. If you have not already renewed your application, please do so as soon as possible. With your early renewal you will continue to receive an uninterrupted subscription to the *Mitochondrion* journal as well as all other membership benefits.

MitoMatters will be published quarterly. The purpose of the MitoMatters is to support the mission of MRS, provide a forum for discussion and report on all aspects of the Society's activity to its members. This publication should also serve as a venue for ideas and concerns, news and discoveries and help integrate our mitochondrial community from around the world. In this issue we have review articles and exciting news reports from both basic and clinical mitochondrial research. We also have sections on funding, society announcements and meetings.

To us mitochondria means the most. So, we invite you to contribute short review articles, news reports and your ideas for future issues of the newsletter to help make this publication a success.

Editors

Andrea Gropman, M.D., Clinical Section
Mariana Gerschenson, Ph. D., Funding Section
Keshav K. Singh, Ph.D., News/Research Report
Nadja C. de Souza Pinto, Ph. D., Meetings/Meeting Report

Managing Editors

Keshav K. Singh, Ph. D.
Nadja C. de Souza Pinto, Ph.D.

Mitochondrial disease in the clinic

Andrea Gropman, M.D.

Despite being the most common of metabolic disorders, mitochondrial cytopathies continue to fascinate clinicians, while at the same time, elude diagnosis in many cases. Since the descriptions of the first cases of mitochondrial disease, tremendous progress has been made in our understanding of this group of disorders including the detailed descriptions of clinical phenotypes, improved methods for diagnosis including greater use of the biochemical and pathology laboratories, immunohistochemical staining, radiology and molecular genetics. This in turn has resulting in defining dozens of mtDNA mutations and a handful of nuclear mutations. On a limited basis, clinical trials have been established in an attempt to palliate clinical symptoms of mitochondrial disease. However, despite tremendous progress, work is still ongoing to fill in our gaps of knowledge.

The heterogeneity of mitochondrial diseases, the hallmark of this group of disorders, is also its downfall. We all are aware that mutations of mtDNA are associated with a wide variety of clinical presentations. The ubiquity of mitochondria and the central role they play in cellular metabolism results in the potential for any tissue to dysfunction in the context of an inborn metabolic defect of the respiratory chain. Although mutations of mtDNA (deletions, duplications, point mutations) have been identified in a high proportion of patients, the role that these play in disease pathogenesis may remain obscure. In addition, of the many patients who present with clinical and laboratory findings suggested of mitochondrial disorders, often mutations have not yet been identified. Phenotypic heterogeneity, intrafamilial and interfamilial variability complicate the diagnosis and genetic counseling of these disorders.

As clinicians invested in the care of patients with mitochondrial disease, we see mitochondrial disease presenting daily in the clinics, in many different ways, some obvious, others more subtle: the infant with encephalopathy and seizures, the older child with developmental delays and possibly autistic features, the adult with neuromuscular disease, the patient with GI dysmotility, the patient presenting to the ophthalmology clinic with poor vision due to optic neuropathy. Patients with mitochondrial disease present to epilepsy clinics, MDA clinics, ophthalmology, GI, pulmonary, and primary care practitioners.

I am delighted to be section editor of the clinical column for MitoMatters. United by our common interest, yet divided geographically, this column can serve an important role in providing information to all those involved in the care of patients with mitochondrial disease. It is my goal in the coming issues to provide the opportunity for exchange of information vital and interesting to those in the mitochondrial community. Such topics will include clinical phenotypes, natural history studies, consensus statements regarding diagnosis, new methods in diagnosis, new mutations, clinical studies recruiting patients, breaking news from scientific meetings with information relevant to mitochondrial disorders. Equally important aspects include issues of nutrition, ethics, genetic counseling and healthcare legislation. From time to time, I will be calling upon the members of the mitochondrial community to contribute to the column and keep this a vibrant forum for the exchange of clinical information. In closing, I would like to thank all of you for your ongoing commitment to the care of patients with mitochondrial cytopathies, and the important work that you do.

Funding for Mitochondrial Research –Getting Started

Mariana Gerschenson, Ph.D.

Welcome to the Mitochondria Research Society Newsletter Column on research funding. The purpose of this column is to guide you to sources of funding, give you information to help you get funded, describe the review process, and explain post-award issues. So where should you start? The first step is to evaluate at what education level you will require funding and to categorize your research interests. What do I mean by research interests? Is your research basic science, translational (pre-clinical), or clinical? You then need to identify your research area by biomedical relevance, e.g. neurological, cardiovascular, cancer etc. Funding for research is either from the government (federal or state), private institutions, or companies in the forms of grants, cooperative agreements, or contracts.

Most scientists are familiar with funding at the government level from both the National Institutes of Health (NIH) (http://www.nih.gov) and the National Science Foundation (NSF) (http://www.nsf.gov/). The NIH grants and contracts web page at http://grants.nih.gov/grants/index.cfm does a good job of supplying general NIH funding information. NIH is comprised of 27 centers and institutes. A summary and description of each institute (e.g. alternative medicine, bioengineering, eye, etc.) is located at http://www.nih.gov/icd/programs.htm. Your application for funding will be assigned to one of these institutes and each institute has different pay lines so knowing the institute's web site is helpful. The NSF also has a web page with a step-by-step guide explaining how to apply for funding (http://www.nsf.gov/home/programs/guide.htm) and you can even apply electronically. NSF also has program areas such as biology, geosciences, and education, etc. where grants are assigned.

Universities also have sources to direct students, postdoctoral fellows, and investigators to apply. The University of California at Berkeley has a web page: http://www.chance.berkeley.edu /research/Funding/ with links to GrantsNet (http://www.grantsnet.org/, a search engines for grants, as well as to the Howard Hughes Medical Institute (http://www.hhmi.org/) and the American Association for the Advancement of Science (http://www.aaas.org/). Foundations are another source for funding and a list of organizations with links can be found at http://www.spo.berkeley.edu/Links/NonprofitWWW.html. Recently (July 31, 2001), the National Organization for Rare Disorders, Inc. (NORD) advertised one-year grant for clinical research studies related to early detection, diagnosis, or treatment of patients with Kearns-Sayre Syndrome (KSS) for $30,000 (orphan@rarediseases.org). The Seek a Miracle Fund announced on September 1, 2001 that there are grant funds available (email Marilyn Downing at Mdown4@aol.com). The Seek a Miracle Fund works in conjunction with the Muscular Dystrophy Association and the Friedreich's Ataxia Research Alliance (http://www. frda.org).

Industry has funding mechanisms in the forms of collaborations, grants, and internships. For instance, GlaxoSmithkline has an internship program at http: //corp.gsk.com/join/university_us.htm., Dupont at http://www.dupont.com/corp/careers/path.html and Abbott Laboratories at http://abbott.com/career/career_center.cfm. Industrial awards are advertised in scientific journals like, 'Science Magazine' or by collaborating/ interacting with industry scientists.

This brief list of web pages should get the novice started on where to find funding. Future topics in this column will include detailed methodology based on your level of education on: how to prepare your application, reviewer selection, what happens during a review, and how funding decisions are made. As we all know, obtaining research funding is difficult enough and being even a little bit more knowledgeable can only help.

News-in-Brief

The Mitochondria Research Society recently sponsored a symposium "Mito 2001: Yeast as a model for mitochondria related human disoders". The meeting took place in the beautiful city of Prague, Czech Republic. The symposium attracted researchers from around the world working on many aspects of mitochondrial diseases and researchers working on molecular biology of yeast mitochondria. Many thanks to the organizers Drs. J. Houstek (Prague) and J. Kolarov (Slovakia) for providing the forum for all of us to come together, and to the people of Prague for their great hospitality. This symposium was organized in honor of Dr. Piotr Slominski, a poet, philospher, and great *mitochondriac* whose contributions to the field is too many to list here.

Piotr Slominski in the middle

Group photo

The Mitochondria Research Society organized its Mitochondria 2001 meeting together with the Mitochondrial Medicine Society (MMS) in San Diego, California, USA. Approximately 200 scientists from around the world attended the meeting. We thank Drs. Richard Haas and Bob Naviaux for their effort in organizing an excellent meeting. Due to their effort, Mitochondria - 2001 was a news item on San Diego NBC television affiliate.

Research-in-Focus

ATP signals pain

We all experience pain one time or the other. It may due to inflammation or tissue damage. In the past years, several molecules such as bradykinin, histamine, prostaglandin and substance P have been described as candidates for sensing pain. However, Cockayne et al and Souslova et al report that ATP binding to the P2X3 receptor- a ATP gated cation-selective ion channel triggers the sensation of pain. This study should help in development of new generation of pain killers.

1. Cokayne DA et al (2000) Urinary hyporeflexia and reduced pain-related behiouour in P2X3-deficient mice. Nature 407:1011-1015.
2. Souslova V et al (2000) Warm-coding deficient and abberant inflammatory pain in mice lacking P2X3 receptors. Nature 407:1015-1017.

Laser Treatment (of mitochondria) reduces scars after heart attack

Low energy laser irradiation of mitochondria appears to reduce the severity of scars and a heart attack. Dr. Uri Oron of Tel Aviv University report that laser treatment after myocardial infarction significantly decreased the size of the scar and lessened the severity of a heart attack by increasing mitochondrial respiration and ATP. Increase in mitochondrial activity by laser irradiation is believed to improve wound healing and muscle regeneration after cardiac injury.

1. Yaakobi T, et al (2001) Long-term effect of low energy laser irradiation on infarction and reperfusion injury in the rat heart. Appl Physiol 90:2411-9
2. Ad N, and Oron U. (2001) Impact of low level laser irradiation on infarct size in the rat following myocardial infarction. Int J Cardiol 80:109-16

Mitochondria and inherited Cancer

A carotid body is a small organ located in the carotid artery in he neck. Paraganglioma tumors occur in carotid body. A study led by Dr Bernie Devlin at Univeristy of Pittsburg reported that inherited paraganglioma is due to a mutation in the succinate-ubiquinone oxido-reductase gene (SDHD). The SDHD protein localizes to mitochondria and is an integral part of mitochondrial complex II.

1. Baysal BE, et al (2000) Mutations in SDHD, a mitochondrial complex II gene, in hereditary paraganglioma. Science 287:848-51

Mito way of starving tumors to death

Angiostatin controls angiogenesis, the process of creating new blood vessel. Angiostatin binds ATP-synthase, a mitochondrial enzyme. ATP-synthase also localizes to the surface of endothelial cells. Dr. Pizzo group reports that ATP-synthase functions as a receptor for angiostatin. This study should advance the development of cancer therapy that cuts off blood supply to tumors.

1. Moser TL, et al (2001) Endothelial cell surface F1-F0 ATP synthase is active in ATP synthesis and is inhibited by angiostatin. Proc Natl Acad Sci U S A 98:6656-61
2. Moser TL et al (1999) Angiostatin binds ATP synthase on the surface of human endothelial cells. Proc Natl Acad Sci U S A 96:2811-6

Upcoming meetings

Feb 10-15, 2002	Gordon Research Conference on Oxygen Radicals Visit www.grc.org for details
April 6-11, 2002	Keystone Symposium on Mitochondria and Pathogenesis. Visit www.keystonesymposia.com
April 30-May 3, 2002	First International conference on NAD(P)H Oxidases.Visit www.med-uni-giessen.de/rbi/noxmeeting
August 25-24,2002	Gordon Research Conference on Mitochondria and Chloroplast. Visit ww.grc.org
October 9-11, 2002	Mitochondria Research Society meeting in Moscow, Russia. Visit http://www.pediatr.mtu-net.ru/News-eng/News.html

International chapters

This year MRS opened international chapters in Czech/Slovak Republic, Denmark, and Russia. If you are interested in starting a MRS chapter in your country, please contact Keshav Singh, Founder, Mitochondria Research Society at singhke@jhmi.edu, Phone 410-614-5128 or Fax 410-502-7234.

Our Sponsors

We thank our sponsors for their contined support of the MRS mission. Their financial help is greatly appreciated.

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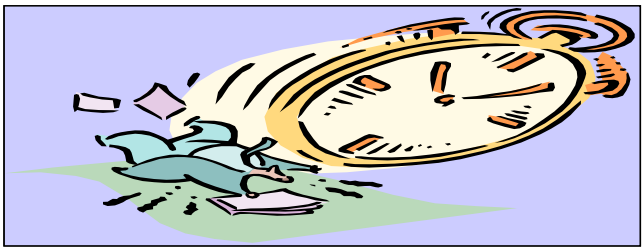

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